

CLAIMS

What is claimed is:

1. A compound comprising a metal complexed with a chelating group
5 attached to a gastrin releasing peptide (GRP) receptor agonist which includes a bombesin
agonist binding moiety.
2. The compound according to claim 1, wherein said compound has a
structure of the formula X-Y-B wherein X is a metal chelating group, Y is a spacer group or
covalent bond and B is a gastrin releasing peptide receptor agonist which includes a
10 bombesin agonist binding moiety.
3. The compound of claim 2 wherein Y is selected from the group
consisting of at least one amino acid residue, a hydrocarbon chain and a combination thereof.
4. The compound of claim 2 wherein X is selected from the group
consisting of DOTA, DTPA, S4, N3S, N2S2, NS3 and derivatives thereof.
- 15 5. The compound of claim 4 wherein Y is selected from the group
consisting of at least one amino acid residue, a hydrocarbon chain and a combination thereof
and B is selected from the group consisting of BBN(7-14) and BBN(8-14).
6. The compound of claim 4 wherein X is DOTA or a derivative thereof.
7. The compound of claim 6 wherein Y is selected is selected from the
20 group consisting of at least one amino acid residue, a hydrocarbon chain and a combination
thereof and B is selected from the group consisting of BBN(7-14) and BBN(8-14).
8. The compound of claim 7 wherein Y is a combination of L-glutamine
and a hydrocarbon chain.
9. The compound of claim 8 wherein Y is a combination of L-glutamine
25 and a C1 to C10 hydrocarbon chain.
10. The compound of claim 9 wherein Y is selected from the group
consisting of glycine, β -alanine, gamma-aminobutanoic acid, 5-aminovaleric acid (5-Ava), 6-
aminohexanoic acid, 7-aminoheptanoic acid, 8-aminooctanoic acid (8-Aoc), 9-aminononanoic
acid, 10-aminodecanoic acid and 11-aminoundecanoic acid (11-Aun).
- 30 11. The compound of claim 4 wherein X is N3S or a derivative thereof.
12. The compound of claim 11 wherein Y is selected from the group
consisting of at least one amino acid residue, a hydrocarbon chain and a combination thereof
and B is selected from the group consisting of BBN(7-14) and BBN(8-14).
13. The compound of claim 12 wherein Y is gly-ser-gly.
- 35 14. A complex comprising a metal and a compound having a structure of
the formula X-Y-B wherein X is a metal chelating group, Y is a spacer group or covalent bond

and B is a gastrin releasing peptide receptor agonist which includes a bombesin agonist binding moiety.

5 15. The complex of claim 14 wherein the metal is selected from the group consisting of transition metals, lanthanides, auger-electron emitting isotopes, and α -, β - or γ -emitting isotopes.

16. The complex of claim 14 wherein the metal is selected from the group consisting of: ^{105}Rh -, $^{99\text{m}}\text{Tc}$ -, $^{186/188}\text{Re}$ -, ^{153}Sm -, ^{166}Ho -, ^{111}In -, $^{90\text{Y}}$ -, ^{177}Lu -, ^{149}Pm -, ^{166}Dy -, ^{175}Yb -, ^{199}Au - and $^{117\text{m}}\text{Sn}$ -.

10 17. The complex of claim 16 wherein X is selected from the group consisting of DOTA, DTPA, S4, N3S, N2S2, NS3 and derivatives thereof.

18. The complex of claim 17 wherein Y is selected from the group consisting of at least one amino acid residue, a hydrocarbon chain and a combination thereof and B is selected from the group consisting of BBN(7-14) and BBN(8-14).

15 19. The complex of claim 16 wherein X is DOTA or a derivative thereof.

20. The complex of claim 19 wherein Y is selected is selected from the group consisting of at least one amino acid residue, a hydrocarbon chain and a combination thereof and B is selected from the group consisting of BBN(7-14) and BBN(8-14).

21. The complex of claim 20 wherein Y is a combination of L-glutamine and a hydrocarbon chain.

20 22. The complex of claim 21 wherein Y is a combination of L-glutamine and a C1 to C10 hydrocarbon chain.

23. The complex of claim 22 wherein Y is selected from the group consisting of glycine, β -alanine, gamma-aminobutanoic acid, 5-aminovaleric acid (5-Ava), 6-aminohexanoic acid, 7-aminoheptanoic acid, 8-aminooctanoic acid (8-Aoc), 9-aminononanoic acid, 10-aminodecanoic acid and 11-aminoundecanoic acid (11-Aun).

24. The complex of claim 23 wherein Y is 8-aminooctanoic acid.

25. The complex of claim 23 consisting of $^{90\text{Y}}$ -DOTA-8-Aoc-BBN(7-14)NH₂.

30 26. The complex of claim 23 consisting of ^{111}In -DOTA-8-Aoc-BBN(7-14) NH₂.

27. The complex of claim 23 consisting of ^{177}Lu -DOTA-8-Aoc-BBN(7-14) NH₂.

28. The complex of claim 23 consisting of ^{149}Pm -DOTA-8-Aoc-BBN(7-14) NH₂.

35 29. The complex of claim 23 consisting of $^{90\text{Y}}$ -DOTA-5-Ava-BBN(7-14)NH₂.

30. The complex of claim 23 consisting of ^{111}In -DOTA-5-Ava-BBN(7-14) NH₂.
31. The complex of claim 23 consisting of ^{177}Lu -DOTA-5-Ava-BBN(7-14) NH₂.
- 5 32. The complex of claim 23 consisting of ^{149}Pm -DOTA-5-Ava-BBN(7-14) NH₂.
33. The complex of claim 16 wherein X is N3S or a derivative thereof.
34. The complex of claim 33 wherein Y is selected from the group consisting of at least one amino acid residue, a hydrocarbon chain and a combination thereof and B is selected from the group consisting of BBN(7-14) and BBN(8-14).
- 10 35. The complex of claim 34 wherein Y is gly-ser-gly.
36. The complex of claim 34 consisting of $^{99\text{m}}\text{Tc}$ -N3S-gly-ser-gly-BBN(7-14)NH₂.
37. A method of treating patient using radioisotope therapy by administering an effective amount of a pharmaceutical comprising a metal complex with a chelating group with a gastrin releasing peptide receptor agonist which includes a bombesin agonist moiety.
- 15 38. The method according to claim 37, wherein said method includes administering an effective amount of a complex comprising a metal and a compound having a structure of the formula
- 20
$$\text{X-Y-B}$$
wherein X is a metal chelating group, Y is a spacer group or covalent bond and B is a gastrin releasing peptide receptor agonist which includes a bombesin agonist binding moiety.
- 25 39. The method of claim 38 wherein the metal is selected from the group consisting of transition metals, lanthanides, auger-electron emitting isotopes, and α -, β - or γ -emitting isotopes.
40. The method of claim 38 wherein the metal is selected from the group consisting of: ^{105}Rh -, $^{99\text{m}}\text{Tc}$ -, $^{186/188}\text{Re}$ -, ^{153}Sm -, ^{166}Ho -, ^{111}In -, $^{90\text{Y}}$ -, ^{177}Lu -, ^{149}Pm -, ^{166}Dy -, ^{175}Yb -, ^{199}Au - and $^{117\text{m}}\text{Sn}$ -.
- 30 41. The method of claim 40 wherein X is selected from the group consisting of DOTA, DTPA, S4, N3S, N2S2, NS3 and derivatives thereof.
42. The method of claim 41 wherein X is DOTA or a derivative thereof.
43. The method of claim 42 wherein Y is selected from the group consisting of at least one amino acid residue, a hydrocarbon chain and a combination thereof and B is selected from the group consisting of BBN(7-14) and BBN(8-14).
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44. The method of claim 43 wherein Y is a combination of L-glutamine and a hydrocarbon chain.

45. The method of claim 44 wherein Y is selected from the group consisting of glycine, β -alanine, gamma-aminobutanoic acid, 5-aminovaleric acid (5-Ava), 6-aminohexanoic acid, 7-aminoheptanoic acid, 8-aminooctanoic acid (8-Aoc), 9-aminononanoic acid, 10-aminodecanoic acid and 11-aminoundecanoic acid (11-Aun).

46. A method of imaging a patient by administering to a subject a diagnostically effective amount of a compound as set forth in claim 1.

47. The method of claim 46, wherein said method includes administering an effective amount of a complex comprising a metal and a compound having a structure of the formula



wherein X is a metal chelating group, Y is a spacer group or covalent bond and B is a gastrin releasing peptide receptor agonist which includes a bombesin agonist binding moiety.

48. The method of claim 47 wherein the metal is selected from the group consisting of transition metals, lanthanides, auger-electron emitting isotopes, and α -, β - or γ -emitting isotopes.

49. The method of claim 48 wherein X is selected from the group consisting of DOTA, DTPA, S4, N3S, N2S2, NS3 and derivatives thereof.

50. The method of claim claim 49 wherein X is N3S or a derivative thereof.

51. The method of claim 50 wherein Y is selected is selected from the group consisting of at least one amino acid residue, a hydrocarbon chain and a combination thereof and B is selected from the group consisting of BBN(7-14) and BBN(8-14).

52. The method of claim 51 wherein Y is gly-ser-gly.

53. A method of forming a therapeutic or diagnostic compound comprising the step of reacting a metal complexed with a chelating group with a gastrin releasing peptide receptor agonist which includes a bombesin agonist moiety.

54. The method of claim 53, wherein said method includes reacting a metal with a compound having a structure of the formula



wherein X is a metal chelating group, Y is a spacer group or covalent bond and B is a gastrin releasing peptide receptor agonist which includes a bombesin agonist binding moiety.

55. The method of claim 54 wherein the metal is selected from the group consisting of transition metals, lanthanides, auger-electron emitting isotopes, and α -, β - or γ -emitting isotopes.

56. The method of claim 54 wherein the metal is selected from the group consisting of: ^{99m}Tc - and $^{186/188}\text{Re}$ -.

57. The method of claim 56 wherein Y is selected is selected from the group consisting of at least one amino acid residue, a hydrocarbon chain and a combination thereof.

58. The method of claim 57 wherein X is selected from the group consisting of DOTA, DTPA, S4, N3S, N2S2, NS3 and derivatives thereof.

59. The method of claim 58 wherein B is selected from the group consisting of BBN(7-14) and BBN(8-14).

60. The method of claim 59 wherein X is DOTA or a derivative thereof and Y is selected from the group consisting of glycine, β -alanine, gamma-aminobutanoic acid, 5-aminovaleric acid (5-Ava), 6-aminohexanoic acid, 7-aminoheptanoic acid, 8-aminooctanoic acid (8-Aoc), 9-aminononanoic acid, 10-aminodecanoic acid and 11-aminoundecanoic acid (11-Aun).

61. The method of claim 59 wherein X is N3S or a derivative thereof and Y is gly-ser-gly.